

### **REMARKS**

Claims 17-26, 29-34 and 37-52 were pending in the subject application. Applicants have amended claims 39, 40, 43, 46, 47 and 50, and cancelled claims 17-26, 29-34, and 37. Claims 1-16 were previously cancelled.

Amended claim 38 places the subject matter in more commonly acceptable form.

Support for amended Claims 39, 40 and 43 may be found in the specification, for example, on page 5, line 17 through page 6, line 20, and page 19, lines 16-20.

Support for amended Claims 46, 47 and 50 may be found in the specification, for example, on page 19, lines 16-20.

The amendments to the claims raise no issue of new matter, and Applicants respectfully request that the amendment be entered.

#### **I. Claims are novel**

##### **A. 35 U.S.C §102(e): Claims 17-26, 28-34, 37, and 39-52.**

On page 2 of the Office Action (see bullet number 3), the Examiner rejected claims 17-26, 28-34, 37, and 39-52 under 35 U.S.C. 102(e) as being allegedly anticipated by Rubland et al. US 7,138,407 (hereinafter referred to as "'407'"), US 7,144,884 (hereinafter referred to as "'884'"), or US 7,148,238 (hereinafter referred to as "'238'") (hereinafter referred to together as "the Rubland patents"). The Examiner is respectfully mistaken and reconsideration thereof is requested.

For prior art to anticipate the present invention, it must be a single piece of prior art that teaches each and every element of the claimed invention. Here, the Examiner alleged that '407, '884, and '238 disclose 4-[2-(4-methylphenylsulfanyl)-phenyl]-piperidine at col. 4, line 48 and each reference also discloses a small genus of compounds explicitly delineated at col. 4, lines 7-48, among which is 4-[2-(4-Chlorophenylsulfanyl)-phenyl]-piperazine at line 21. The Examiner then concluded that the instant claims are anticipated by each reference because the compounds of the references were sufficiently limited and well delineated with "modifications of two species to arrive at the species of the instant claims".

Applicants maintain that '407, '884, and '238 each fail to teach each and every aspect of the present invention. For example, amended claim 38 reads:

A compound selected from the group consisting of:  
4-[2-(2-Fluoro-phenylsulfanyl)-6-fluoro-phenyl]-piperidine;  
4-[2-(4-Chloro-2-fluoro-phenylsulfanyl)-6-fluoro-phenyl]-piperidine;  
4-[2-(3-Chloro-2-fluoro-phenylsulfanyl)-6-fluoro-phenyl]-piperidine;  
4-[2-(2-Fluoro-4-methyl-phenylsulfanyl)-6-fluoro-phenyl]-piperidine;  
4-[2-(2-Fluoro-4-methoxy-phenylsulfanyl)-6-fluoro-phenyl]-  
piperidine;  
4-[2-(2,4-Difluoro-phenylsulfanyl)-6-fluoro-phenyl]-piperidine; and a  
pharmaceutically acceptable salt thereof.

Clearly, '407, '884, and '238 **do not teach any** of the specific compounds claimed in claim 38 above, and thus do not anticipate the present invention. In fact, the Examiner has acknowledged that each reference does not teach each and every aspect of the present invention, because in the Examiner's alleged basis for her 102 rejection, the Examiner has stated that two species of each reference must be **modified** to arrive at the instant claims. If modification of the reference compounds is needed, each reference cannot teach each and every aspect of the instant claims.

Accordingly, the instant claims are novel, and applicants respectfully request the Examiner reconsider and withdraw this rejection.

B. 35 U.S.C. §102(f),(g): Claims 17-26, 28-34, 37, and 37-52.

On Page 6, of the Office Action (see bullet number 9), the Examiner again alleged that claims 17-26, 28-34, and 37-52 are directed to the same invention as that of '407, '884, or '238, and thus, are anticipated as discussed above and have a priority issue under 35 U.S.C. §102(g) and possibly 35 U.S.C. §102(f) that must be resolved.

In light of the remarks made hereinabove regarding the rejection under 35 U.S.C. §102(e), this objection is moot. In other words, because 407, '884, or '238 do not anticipate the instant claims, there is no priority issue.

Additionally, the undersigned, under 35 U.S.C. §103(c), provides that:

**The present Patent Application No. 10/551,883 and US Patent Nos. 7,138,407, 7,144,884 and 7,148,238 were, at the time the invention of Patent Application No. 10/551,883 was made, owned by H. Lundbeck A/S.**

Accordingly, Applicants respectfully request that the Examiner acknowledge that the alleged priority issue has been resolved.

## **II. Claims are unobvious**

### **A. 35 U.S.C. §103(a): Claims 17-26, 28-34 and 38.**

On page 2 of the Office Action (see bullet number 2), the Examiner rejected claims 17-26, 28-34 and 38 under 35 U.S.C. §103(a) as allegedly being unpatentable over Ong & Proffitt's US 4,198,419 (hereinafter referred to as '419) supplemented with CA 93:71569. The Examiner is respectfully mistaken and Applicants request reconsideration thereof.

The Examiner alleged that '419 discloses "RN 74442-94-7 as a synthetic intermediate for making the claimed compounds" as RN 74442-94-7 is an "N-protected compound of the instant claim 38" and the currently amended multiple substituted compounds are generically taught by '419. The Examiner then concluded that "N-protection and its hydrolyzed modifications are considered prima facie obvious in the chemical art, especially variations of protected compounds, which were disclosed by the reference for making the piperidine free base."

However, '419 **does not** disclose intermediates for making compounds of the present invention. In fact, it discloses intermediates to **spiro[dibenz[b,f]-thienpin-piperidine]s**, which are described in Ong & Proffitt's simultaneously filed application to same that issued as US Patent No. 4,198,420. See, e.g., col. 1, lines 9-15 of '419. Clearly, the teaching and scope of '419 is for phenylthienophenylpiperidines as intermediates to spiro[dibenz[b,f]-thienpin-piperidine]s and not to the instantly claimed 4-(2-phenylsulfanyphenyl)-piperidines.

Also, '419 discloses compounds that **require** substitution in the 4<sup>th</sup> position of the piperidine ring with an R' moiety, wherein R' is cyano, COOH, COZ, lower alkanoyl or lower alkoxy carbonyl. See e.g., claims 1-39 and 41-73, col. 1, lines 16-43, and col. 4 through col. 8, line 33. By contrast, the compounds of the present invention **do not require** substitution at the 4<sup>th</sup> position of the piperidine ring. See e.g., amended claim 38.

Moreover, though the compound RN 74442-94-7 is claimed in '491, it appears to be misidentified and misclaimed. Claims 17 to 51 of '419 correspond to the Examples disclosed at col. 9, line 24 through col. 19, line 52, except for Examples 23, 25 and 26, which are not specifically claimed. Example 25 discloses the 4-carboxylic acid of RN 74442-94-7. Claim 40 directed to RN 74442-94-7 likely was meant to cover Example 25, i.e., the 4-carboxylic acid of RN 74442-94-7, because as previously discussed '419 is directed to 4-substituted-phenylthiophenyl-piperidines and other 4-carboxylic acid Examples are claimed. See e.g., claims 18, 30, 31, 42, 45 and 46. Undoubtedly then, it appears that the claiming of RN 74442-94-7 was erroneous and not within the full scope of '419.

Additionally, the mere claiming of RN 74442-94-7 in '419 does not make the instant compounds obvious. Prior art must be viewed for all that it teaches. Picking and choosing elements from prior art to achieve the claimed invention is improper when not viewed within the full scope of the prior art. See *In re Wesslau*, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965) (finding it impermissible to "pick and choose" from any reference only so much of it as to support a given position to the exclusion of other parts of the reference so as to limit the full appreciate of what the reference suggests). Here, again, '419 teaches (i.e., the scope of '419 is), 4-substituted-phenylthiophenyl-piperidine intermediates to spiro[dibenz[b,f]-thienpin-piperidine]s. It clearly fails to teach, much less suggest or motivate, one skilled in the art to identify RN 74442-94-7 among all the 4-substituted piperidine compounds disclosed, and make the necessary modifications to arrive at the compounds of the present invention. In fact, the subject matter ("the 14<sup>th</sup> compound") for which RN 74442-94-7 is the closest prior art is not under examination, which the Examiner even acknowledged. See e.g., page 2 of the Office Action.

Furthermore, though '419 discloses a number of N-protected piperidines, it fails to disclose those for compounds of amended claim 38 – namely:

4-[2-(2-Fluoro-phenylsulfanyl)-6-fluoro-phenyl]-piperidine;  
4-[2-(4-Chloro-2-fluoro-phenylsulfanyl)-6-fluoro-phenyl]-piperidine;  
4-[2-(3-Chloro-2-fluoro-phenylsulfanyl)-6-fluoro-phenyl]-piperidine;  
4-[2-(2-Fluoro-4-methyl-phenylsulfanyl)-6-fluoro-phenyl]-piperidine;  
4-[2-(2-Fluoro-4-methoxy-phenylsulfanyl)-6-fluoro-phenyl]-  
piperidine; and  
4-[2-(2,4-Difluoro-phenylsulfanyl)-6-fluoro-phenyl]-piperidine.

Consequently, one skilled in the art searching for ways to arrive at the compounds of the present invention would not have any reason to select '419 as a guide to making the instant invention. The claimed compounds therefore are non-obvious.

For the foregoing reasons, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

B. 35 U.S.C. §103(a): Claims 17-26, 28-34, and 37-52.

On page 3 of the Office Action (see bullet number 4), the Examiner rejected claims 17-26, 28-34, and 37-52 under 35 U.S.C. §103(a) as being allegedly unpatentable over '407, '884, or '238. The Examiner is respectfully mistaken and reconsideration thereof is requested.

The Examiner alleged that references '407, '884, and '238 disclose the 4-[2-(4-methylphenylsulfanyl)-phenyl]-piperidine and that each reference also discloses a small genus of compounds among which 4-[2-(4-Chloro-phenylsulfanyl)-phenyl]-piperazine and 23 other compounds allegedly clearly delineate the variation of mono, or di- or tri-substitution on the phenylsulfanylphenyl system. In view of this, the Examiner alleged that one having ordinary skill in the art in possession of '407, '884, and '238 would be motivated to pick and choose any combination of the genus of each issued patent guided by the species disclosed therein, and in absence of unexpected results, there is nothing unobvious in picking some among many.

Yet '407, '884, and '238 are not appropriate prior art under 103(c) because (a) as alleged by the Examiner, the rejection is a 102(e)/103 rejection, (b) these references and the claimed invention have three common inventors, and (c) these references and the claimed invention were subject to an obligation of assignment to the same person at the time the claimed invention was made. See e.g. MPEP §2137.01(VI) (providing that a rejection under 102(e)/103 is precluded by 35 U.S.C. 103(c) once proper evidence is made of record).

Accordingly, the undersigned, under 35 U.S.C. §103(c), provides that:

**The present Patent Application No. 10/551,883 and US Patent Nos. 7,138,407, 7,144,884 and 7,148,238 were, at the time the invention of Patent Application No. 10/551,883 was made, subject to an obligation to assign to H. Lundbeck A/S.**

Applicants, therefore, respectfully request that the Examiner reconsider and withdraw this rejection.

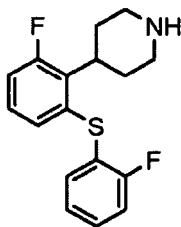
C. 35 U.S.C. §103(a): Claims 17-26, 28-34, and 37-52.

On page 4 of the Office Action (see bullet number 5), the Examiner rejected claims 17-26, 28-34, and 37-52 under 35 U.S.C. §103(a) as being allegedly unpatentable over Rubland et al. US 6,699,864 (hereinafter referred to as '864). The Examiner is respectfully mistaken and reconsideration thereof is requested.

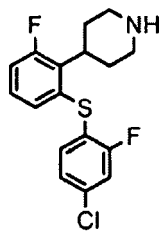
The Examiner alleged that '864 discloses the instantly claimed compounds as intermediates of formula III for making substituted phenyl-piperazines, and since each of the Rubland patents ('238, '407 or '884) evidence that the intermediates would have a separate utility in addition to the utility of being starting material for products of '864, one skilled in the art in possession of the '864's formula III is in possession of the instant claims generically while "making the more limited subgenus or species obvious."

However, '864 does not disclose the instantly claimed compounds as intermediates for making the final products of '864. For instance, the compounds of amended claim 38, namely:

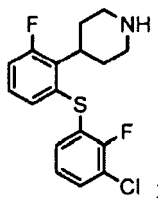
4-[2-(2-Fluoro-phenylsulfanyl)-6-fluoro-phenyl]-piperidine, i.e.,



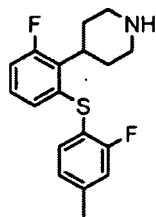
4-[2-(4-Chloro-2-fluoro-phenylsulfanyl)-6-fluoro-phenyl]-piperidine, i.e.,



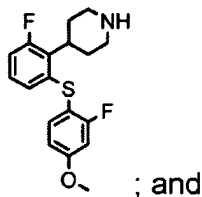
4-[2-(3-Chloro-2-fluoro-phenylsulfanyl)-6-fluoro-phenyl]-piperidine, i.e.,



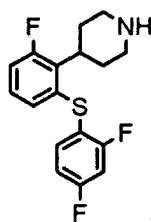
4-[2-(2-Fluoro-4-methyl-phenylsulfanyl)-6-fluoro-phenyl]-piperidine, i.e.,



4-[2-(2-Fluoro-4-methoxy-phenylsulfanyl)-6-fluoro-phenyl]-piperidine, i.e.,



4-[2-(2,4-Difluoro-phenylsulfanyl)-6-fluoro-phenyl]-piperidine, i.e.,



all require fluorine **substitution** at the 6<sup>th</sup> position of the phenyl immediately attached to the 4<sup>th</sup> position of the piperidine ring.

By contrast, the intermediate compounds of formula III of '864 are **unsubstituted** at the same position (see col. 7, lines 53-65). In fact, there is no teaching, suggestion or motivation in '864 to substitute the phenyl immediately attached to the 4<sup>th</sup> position of the piperidine ring, much less to substitute fluorine at the 6<sup>th</sup> position of such phenyl, as is present in the compounds of the instant invention. See e.g., claim 1 and Examples.

Moreover, even though '864 discloses that for intermediates of formula III, X may be sulfur and that Y may be CH, '864 **teaches away** from such compounds. For instance, '864 fails to disclose any of the instantly claimed compounds, which have a piperidine ring, and a sulfur linker between the phenyl rings. Instead '864 provides that the most preferred embodiments of its invention are compounds of the formula I, wherein said compounds have an oxygen linker between the phenyl rings, and Y is nitrogen forming a piperazine ring. See '864, col. 4, lines 25-26 and line 41 through col. 6, line 50. Clearly, the scope of '864 is the provision of substituted-phenoxyphenyl-piperazines and -benzodioxolanyloxyphenyl-piperazines.

Consequently, a skilled person searching for the instantly claimed compounds of the present invention would not be motivated to modify the teachings of '864 to arrive to the instantly claimed compounds. Applicants maintain that the motivation to modify '864 must arise from some teaching or suggestion in the '864 that provides the desirability to make such modification to arrive to the claimed invention. The mere fact that '864 could be modified in such manner would not have made the modification obvious unless the prior art suggest the desirability of the modification, and '864 clearly does not. Rather, '864 **teaches away** from such modification as previously discussed.

Further, Applicants respectfully remind the Examiner that using hindsight in finding the instant invention obvious over the prior art is impermissible. It is impermissible to use the Applicants' invention as a "road map" to piece together the teachings of the prior art in order to render the claimed invention obvious. See, e.g., MPEP §2142 (providing that "impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art"); see also, *KSR Int'l Co. v. Teleflex, Inc.*, at 22 (stating expressly that hindsight analysis of a patent challenged for obviousness is still to be avoided).

Regarding the Rubland patents, '407, '884, and '238, if the Examiner intended to cite these references in combination with '864 for the 103 rejection is unclear as they are not cited basis for the actual rejection. However, if that was the intention of the Examiner, Applicants maintain that '407, '884, and '238 do not cure the deficiencies of '864 with respect to making the instantly claimed compounds obvious. As previously discussed, '407, '884, and '238 are precluded as proper prior art under 103(c) and as evidenced by the undersigned hereinabove.

For the forgoing reasons, applicants respectfully request that the Examiner reconsider and withdraw this rejection.

D. Common Ownership with US Patent No. 6,699,864:

On page 4 of the Office Action (see bullet number 6), the Examiner further alleged that '864 discloses the claimed invention and fully enabled the intermediates, though it did not claim the disclosed intermediates. The Examiner acknowledged that

'864 has a common assignee as the instant application and urged Applicants to provide evidence for the record that the invention of '864 derived from the instant inventor and that '864 and the claimed invention are commonly owned or subject to an obligation of assignment to the same person at the time the claimed invention was made.

In response, in an attempt to advance the prosecution of the subject application, and without conceding the correctness of the Examiner's position with respect to '684, the undersigned, under 35 U.S.C. §103(c), provides that:

**The present Patent Application No. 10/551,883 and  
US Patent No. 6,699,864 were, at the time the  
invention of Patent Application No. 10/551,883  
was made, owned by H. Lundbeck A/S".**

Accordingly, Applicants respectfully request that the Examiner acknowledges same as evidence for the record, and consequently, further reconsider and withdraw the 103 rejection based on '684.

### **III. Claims are patentable:**

#### **A. Claims 17-26, 28-34, and 37-52 patentable over US Patent No. 7,148,238:**

On page 4 of the Office Action (see bullet number 7), the Examiner rejected claims 17-26, 28-34 and 37-52 on the grounds of non-statutory obviousness-type double patenting as being allegedly unpatentable over claims 1-18 of US Patent No. 7,148,238. The Examiner alleged that although the conflicting claims are not identical, they are not patentably distinct from each other because the issued claims contain overlapping compounds with the instant claims, and that the overlapping compounds are obvious variations of the mix and match combination of substituents on the phenylthiophenyl ring system, which therefore, renders the non-overlapping scope prima facie obvious since they differ in explicit/nonexplicit combination of Markush elements.

Merely in an attempt to advance the prosecution of the subject application, and without conceding the correctness of the Examiner's position, applicants enclose a Terminal Disclaimer in compliance with 37 C.F.R. 1.321(c), to overcome this rejection along with the requisite fee of \$140.00.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

B. Claims 17-26, 28-34, and 37-52 patentable over US Patent Nos. 7,138,407, 7,144,884, and 6,699,864:

On page 5 of the Office Action (see bullet number 8), the Examiner rejected claims 17-26, 28-34 and 37-52 on the grounds of non-statutory obviousness-type double patenting as being allegedly unpatentable over claims 1-18 of '407 or claims 1-29 of '884, in view of 864. The Examiner alleged that claims 1-18 of '407 or claims 1-29 of '884 are drawn to piperazinyl ring compounds instead of the instant piperidinyl ring compounds with similar substitution of a phenylthiophenyl at the 4-position, where piperazine and dihydropyridine as an alternative of piperidine is "conventionally" disclosed by the '864 patent; and thus are obvious alternative choices for one having ordinary skill to pick and choose.

At the suggestion of the Examiner, and merely in an attempt to advance the prosecution of the subject application without conceding the correctness of the Examiner's position, Applicants enclose three (3) Terminal Disclaimers in compliance with 37 C.F.R. 1.321(c), to overcome this rejection along with the requisite fees, totaling \$420.00.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

#### **IV. Conclusion**

The Commissioner is hereby authorized to charge the aforementioned fees - \$1,110.00 for the Three-Months Extension of Time and the fee of \$560.00 for the four (4) Terminal Disclaimers - to Deposit Account No. 50-3201. No fee is deemed

necessary in connection with the filing of this response. However, the Commissioner is further authorized to charge any fee or underpayment thereof, or credit any overpayment, to Deposit Account No. 50-3201, as necessary.

In view of the foregoing, Applicants submit that the instant application is in condition for allowance. An early Notice of Allowance is earnestly solicited. Applicants invite the Office to contact the undersigned to discuss any outstanding matters.

Respectfully submitted,

/Margaret M. Buck, Reg. # 54,010/

Margaret M. Buck, Esq.  
Registration No. 54,010

Lundbeck Research USA, Inc.  
215 College Road  
Paramus, New Jersey 07652  
(201) 650-0790 (phone)  
(201) 225-9571 (fax)